REMARKS

Claims 1-8, 10, 12-15, 18, 19 and 50-57 are pending in the present application. Claims 24-44, 48 and 49 were withdrawn by the Examiner from further consideration pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention and are cancelled without prejudice, reserving the right to prosecute the same or similar claims in one or more divisional applications. The limitations of Claims 2 and 4 have been incorporated into Claim 1 in the present Amendment and Response and Claims 2 and 4 are hereby cancelled without prejudice.

Remaining Claims 1, 3, 5-8, 10, 12-15, 18, 19 and 50-57 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification is such a way as to enable one skilled in the art to make and/or use the invention.

In the Advisory Action of January 17, 2003, the most recent Office Action to address the patentability of these claims, the sole issue raised by the Examiner in rejecting these claims under 35 U.S.C. §112 was that he did not conclude that Amendment and Response filed by Applicants on December 9, 2002 showed that the heterologous functional domains provided the claimed improved background specificity. Applicants note that the Examiner now agrees that the specification describes the making and using of a number of enzymes having improved background specificity over the strains from which they were made (June 3, 2003 Office Action at page 2), thus removing the grounds for the previous rejection under 35 U.S.C. §112.

The Examiner maintains a rejection under 35 U.S.C. §112, and now asserts that Applicants have not provided a general teaching of how to make such enzymes (Office Action at page 3). The Examiner asserts that Applicants have not enabled one of ordinary skill in the art to make all such enzymes, and that Applicants have enabled one of ordinary skill to make only certain enzymes that have improved background specificity (Office Action at page 2) .

Applicants have provided a general description of the method of identifying functional domains in enzymes and constructing recombinant enzymes comprising heterologous functional domains having improved activities (see, *e.g.*, pages 35 to 49 of the specification, described in more detail, below). However, for business reasons and without acquiescing to

the Examiner's arguments, and reserving the right to pursue the original or similar claims in the future, Applicants have amended the present claims to recite a composition comprising a polymerase comprising a 5' nuclease, wherein the polymerase enzyme comprises a heterologous functional domain, wherein the heterologous functional domain comprises an amino acid sequence that provides improved background specificity in a nucleic acid cleavage assay compared to the polymerase enzyme without the heterologous functional domain.

The instant application provides general instructions of how to make the claimed compositions comprising a polymerase enzyme comprising a 5' nuclease. As noted on page 35 at lines 11-17, the methods used in creating and selecting the improved compositions of the present invention are described in detail in both the Detailed Description of the Invention and in the experimental examples. Examples of the specific teachings are included in the following sections: I) Creation and selection of chimerical constructs (page 35, line 19 to page 37, line 19) ; II) Site-specific mutagenesis based on information from chimerical constructs (page 37, line 20 to page 38, line 28); III) Site-specific mutagenesis based on molecular modeling and published physical studies (page 39, line 1 to page 47, line 17) ; and IV) focused random mutagenesis (page 47, line 19 to page 49, line 13). These sections provide extensive analysis of the characteristics of polymerase enzymes (see, *e.g.*, section III in its entirety), instructions on how to identify regions of such polymerases linked to the particular activities (see, e.g., section I in its entirety), and instruction on how the claimed improvements can be conferred on polymerase enzymes by providing heterologous functional domains (see, *e.g.*, sections I through IV).

As noted in the Amendment and Response filed in this case on April 7, 2003, and incorporated by reference herein, Applicants have also provided a general procedure for screening and characterizing the cleavage activity of any polymerase comprising a heterologous functional domain, so as to allow one of skill in the art to identify compositions providing improved background specificity in a nucleic acid cleavage assay.

The present application thus provides general instructions allowing those skilled in the art to construct the particular polymerase enzymes described by the Applicants, and additional such polymerase enzymes having the claimed improvements in activity. The present application also provides detailed testing methods to allow one of skill in the art to identify,

without undue experimentation, additional polymerase enzymes having the claimed improvements.

As detailed above, the subject matter of Claims 1, 3, 5-8, 10, 12-15, 18, 19 and 50-57 is described in the specification is such a way as to enable one skilled in the art to make and use the invention. As such, Applicants assert that the present application clearly satisfies the requirements of 35 U.S.C. §112, first paragraph cited by the Examiner as his basis for this rejection. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants' claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 218-6900.

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